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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/667,783

09/23/2003

Miroslav Smriga

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EXAMINER

ROBERTS, LEZAH

ART UNIT

PAPER NUMBER

1614

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

01/29/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/667,783

Applicant(s)

SMRIGA ET AL.

Examiner

Lezah W. Roberts

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1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 October 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 24-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date A-C.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION

Response to Election of Species and Restriction Requirement

Claims 24-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on October 25, 2006.

Applicant's election with traverse of stress-induced diseases in the reply filed on October 25, 2006 is acknowledged. The traversal is on the ground(s) that the Examiner has not provided any reasons or examples to support a conclusion that the species are patentably distinct. A search of all the claims would not impose a serious burden on the Office. This is not found persuasive because the different diseases have different etiologies thereby require different regimens of treatment.

The requirement is still deemed proper and is therefore made FINAL.

Claims

Claim Rejections - 35 USC § 112 – Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for ameliorating, progress blocking and therapeutically treating one or more stress induced diseases, does not reasonably provide enablement for preventing one or more stress induced diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

- 1) the nature of the invention,
- 2) the breadth of the claims
- 3) the relative skill of those in the art,
- 4) the state of the prior art,
- 5) the predictability of the art,
- 6) the amount of direction or guidance provided,
- 7) the presence or absence of working examples, and
- 8) the quantity of experimentation necessary,

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth infra.

1) *The nature of the invention.* The invention discloses using a composition comprising lysine to therapeutically treat stress-induced diseases.

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2) *The breadth of the claims.* The claims are broad because they read on "preventing".

3) *The relative skill of those in the art.* The relative skill of those in the art are PhD, MD, and MS.

4) *The State of the Prior Art.* The prior art discloses that using lysine reduces symptoms and occurrences of stress induced diseases. According to the University of Maryland Medical Center, lysine is important for proper growth and plays an essential role in the production of carnitine, a nutrient responsible for converting fatty acids into energy and helping to lower cholesterol. Lysine appears to help the body absorb and conserve calcium and it plays an important role in the formation of collagen, a substance important for bones and connective tissues including skin, tendon, and cartilage. If there is too little lysine in the diet, kidney stones and other health related problems may develop including fatigue, nausea, dizziness, loss of appetite, agitation, bloodshot eyes, slow growth, anemia, and reproductive disorders. L-lysine can be used to treat mouth and genital lesions caused by herpes simplex virus as well as shingles caused by herpes zoster viruses. Taking lysine supplements can speed recovery time and reduce the chance of recurrent breakouts of the herpes infection. In addition, test tube studies suggest that L-lysine in combination with L-arginine (another amino acid) increases the activity of bone-building cells and enhances production of collagen. Certain forms of lysine and/or lysine bound to anti-inflammatory medications may help alleviate pain following an episiotomy. These forms of lysine may also relieve migraine headaches and painful periods. Whether L-lysine and other readily available lysine

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supplements also offer these benefits is not known

(<http://www.umm.edu/altmed/ConsSupplements/Lysinecs.html>).

5) *The Predictability or Lack Thereof in the Art.* Prevention is not practical with stress induced diseases because there are various types of stressed induce diseases. The administration of a compound to prevent all these diseases is unlikely. Stress induced diseases are caused by stress. Stress is difficult for scientists to define because it is a subjective sensation associated with varied symptoms that differ for each of us. In addition, stress is not always a synonym for distress. Situations like a steep roller coaster ride that cause fear and anxiety for some can prove highly pleasurable for others. Winning a race or election may be more stressful than losing but this is good stress. Increased stress increases productivity – up to a point, after which things rapidly deteriorate, and that level also differs for each of us (<http://www.stress.org>). Because stress is caused by outside factors such as work, school or personal relationships, it would be hard to prevent the resulting conditions from this type of environment without removing these factors from the individual. For instance in the case of anxiety, drugs are used to help numb anxiety, but ultimately, the sufferer has to face the anxiety again when the drugs are withdrawn (<http://www.panic-anxiety.com/anti-anxiety-drug.htm>). This indicates that anxiety can be masked and not prevented. Furthermore diseases such as anxiety can be caused by different events such as life situations may trigger excessive anxiety. For example, having a physical illness, along with the stress of missing work or losing pay, may combine to cause generalized anxiety disorder (<http://www.mayoclinic.com/health/generalized-anxiety->

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disorder/DS00502/DSECTION=3). Vitamin deficiency is just one of the causes of stress-induced disorders such as anxiety. As stated above, lysine has also been used to treat patients with herpes simplex virus type I (HSV). Reactivation of HSV is thought to occur partly from psychological stress (Padgett et al., Proc. Natl. Acad. Sci. USA 95 (1998)). Although lysine reduces the occurrence of outbreaks, it does not prevent them.

6) *The Amount of Direction or Guidance Present.* Applicant provides guidance for ameliorating the conditions for certain stress-induced conditions. The experiments used to test the effects of lysine were controlled experiments where the source of stress was created and not a factor of the environment.

7) *The Presence or Absence of Working Examples.* The disclosure discloses experiments to show the effect of lysine on gastric ulcers, appetite loss, anxiety, irritable colon syndrome, and hypersensitivity. Also disclosed were compositions that are used to treat the above stress-induced diseases.

8) *The Quantity of Experimentation Needed.* The applicant needs to provide examples of using the compositions to treat the animals followed by applying the same stresses on the animal without continuous administration of the drug to determine if the diseases occur. Experiments comprising administering to a patient, with a hectic or stressful lifestyle, the compositions comprising lysine, need to be performed to determine if conditions such as anxiety or hypertension occurs.

Suggested language. Since the term "treatment" is a broad term, it will inherently cover therapies in which some protective function may also be present. Accordingly, the

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examiner recommends simply reciting method for "ameliorating, progress blocking and therapeutically treating one or more stress induced diseases".

2) Claims 1-14 and 16-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for anxiety disorders, dissociated disorders, emotion disorders, abnormal gastric motion, irritable colon syndrome, irritable bowel syndrome and gastric ulcer, does not reasonably provide enablement for all stress induced disorders such as psychosomatic disorders (somatopathy disease of the body), and other diseases such as increased palpitations, heart ailments such as coronary artery disease, headache, sweaty hands & feet and trembling. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

- 1) the nature of the invention,
- 2) the breadth of the claims
- 3) the relative skill of those in the art,
- 4) the state of the prior art,
- 5) the predictability of the art,
- 6) the amount of direction or guidance provided,
- 7) the presence or absence of working examples, and
- 8) the quantity of experimentation necessary,

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The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth infra.

1) *The nature of the invention.* The invention discloses using a composition comprising lysine to therapeutically treat stress-induced diseases.

2) *The breadth of the claims.* The claims are broad because they read on "all stress-induced diseases".

3) *The relative skill of those in the art.* The relative skill of those in the art are PhD, MD, and MS.

4) *The State of the Prior Art.* The prior art discloses that using lysine reduces symptoms and occurrences of stress induced diseases such as anxiety (US 5,505,968). According to the University of Maryland Medical Center, lysine is important for proper growth and plays an essential role in the production of carnitine, a nutrient responsible for converting fatty acids into energy and helping to lower cholesterol. Lysine appears to help the body absorb and conserve calcium and it plays an important role in the formation of collagen, a substance important for bones and connective tissues including skin, tendon, and cartilage. If there is too little lysine in the diet, kidney stones and other health related problems may develop including fatigue, nausea, dizziness, loss of appetite, agitation, bloodshot eyes, slow growth, anemia, and reproductive disorders. L-lysine can be used to treat mouth and genital lesions caused by herpes simplex virus as well as shingles caused by herpes zoster viruses. Taking lysine supplements can speed recovery time and reduce the chance of recurrent breakouts of the herpes infection. In

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addition, test tube studies suggest that L-lysine in combination with L-arginine (another amino acid) increases the activity of bone-building cells and enhances production of collagen. Certain forms of lysine and/or lysine bound to anti-inflammatory medications may help alleviate pain following an episiotomy. These forms of lysine may also relieve migraine headaches and painful periods. Whether L-lysine and other readily available lysine supplements also offer these benefits is not known

(<http://www.umm.edu/altmed/ConsSupplements/Lysinecs.html>). It has also been reported that compositions with isolated amino acids such as lysine are used in compositions to manage irritable bowel syndrome (US 20050100535 paragraph 0021).

5) *The Predictability or Lack Thereof in the Art.* Stress induced diseases encompasses a multitude of diseases that have not been addressed by the instant disclosure such as increased palpitations, heart ailments such as coronary artery disease, headache, sweaty hands & feet and trembling. Other diseases discussed in the disclosure but not in full detail are psychosomatic disorders (somatopathy, disease of the body, which may encompass anything). Stress is difficult for scientists to define because it is a subjective sensation associated with varied symptoms that differ for each of us. In addition, stress is not always a synonym for distress. Situations like a steep roller coaster ride that cause fear and anxiety for some can prove highly pleasurable for others. Winning a race or election may be more stressful than losing but this is good stress. Increased stress increases productivity – up to a point, after which things rapidly deteriorate, and that level also differs for each of us (<http://www.stress.org>). Because stress is caused by outside factors such as work, school or personal relationships, it

would be hard to prevent the resulting conditions from this type of environment without removing these factors from the individual. For instance in the case of anxiety, drugs are used to help numb anxiety, but ultimately, the sufferer has to face the anxiety again when the drugs are withdrawn (<http://www.panic-anxiety.com/anti-anxiety-drug.htm>).

The risk of an individual having diseases such as stress-induced cardiovascular damage may be increased by a genetic variant (<http://www.dukemednew.org/news/article.php?id=10>). The difference in genetic make up such as differences in alleles of a known variant of the serotonin transporter gene affects the individual's response to mental stress. It cannot be predicted how different individuals with these differences will react to lysine therapy without experimentation. The suggested treatment for this is stress management.

6) *The Amount of Direction or Guidance Present.* Applicant provides guidance for ameliorating the conditions for certain stress-induced diseases. The experiments used to test the effects of lysine were controlled experiments where the source of stress was created and not a factor of the environment.

7) *The Presence or Absence of Working Examples.* The disclosure discloses experiments to show the effect of lysine on gastric ulcers, appetite loss, anxiety, irritable colon syndrome, and hypersensitivity. Also disclosed were compositions that are used to treat the above stress-induced diseases.

8) *The Quantity of Experimentation Needed.* Applicant needs to run experiments showing the effect administering these compositions have on patients prone to coronary heart disease, or diseases and conditions such as palpitations, headache, sweaty

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hands & feet and trembling. Experiments administering lysine to individuals with stressful lifestyles should also be performed to determine if lysine helps the individual cope with stressful situations.

Claim Rejections - 35 USC § 102 - Anticipation

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1) Claims 1-11, 13, 15-20 and 22-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Schaefer et al. (US 5,505,968).

Schaefer et al. disclose compositions as an antemortem, which is an anxiety disorder, nutrient supplement for livestock. The compositions contain one or more sources of electrolytes including sodium, potassium and magnesium, one or more sources of amino acids including lysine and glutamate, all in a bypass form; and a source of tryptophan. Glutamate or glutamic acid is added to the compositions in large quantities to provide an ammonia buffering effect (col. 4, lines 21-33), encompassing claims 7-11. Other beneficial ingredients include arginine. The invention also extends to

methods of administering the supplements to livestock to reduce antemortem stress. Certain bypass amino acids may be supplemented with the food grade chemical forms, where the latter form is economical (col. 5, lines 51-57). These include lysine. Feed grade lysine is available in salt form¹. The amount of feed grade lysine incorporated in the compositions varied. The pellet of Supplement 1(b) comprised 1.5 of lysine and administered to a 500 kg animal. This is equivalent to 0.003 g/kg/body, encompassing claims 16-17. The additional amino acids are also incorporated in components such as corn gluten meal (Table 1(a)), encompassing claims 6 and 10. The supplement of the invention is most preferably administered to the animal in a solid form, in admixture with the normal feed. Alternatively, the composition may be provided in a liquid form as a liquid consumable or drench. The solid product is preferably formulated with typical feed carriers and binders, known in the animal feedstuffs industry. The feed is administered prior to transport as a preventive step (col. 2, lines 20-37), encompassing claim 13. Salts in the invention include NaCl and MgSO₄, encompassing claim 22. The reference anticipates the claims insofar as it discloses a method of reducing antemortem stress by feeding livestock a composition comprising lysine and another amino acid.

2) Claims 1 and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Houston (6,447,772).

¹ Alibaba.com http://www.alibaba.com/manufacturer/14615384/Sell_Feed_Grade_L_Lysine_Hcl.html, pages 1-2, 1999

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Houston discloses compositions to treat symptoms of autism in humans (see abstract). These symptoms include anxiety. The compositions comprise lysine (see example 2) encompassing the instant claims. The reference anticipates the instant claims insofar as it discloses a compositions comprising lysine that treats stress-induced diseases such as anxiety disorders.

3) Claims 1-4, 13-17 and 20-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Pitman (US 2004/0005311).

Pitman discloses a dietary supplement composition comprising lysine. Patients that are lysine deficient took the compositions. Patients experiencing anxiety and memory loss took the composition and the symptoms were decreased. Patients that continued taking a combination of lycopene and lysine continued to exhibit reduced symptoms (paragraph 0073). The amount of lysine taken per day ranges from 500 to 7500 mg, therefore based on a 75 kg patient, the dosage would range from 0.0067 to 0.1 g/kg encompassing claims 16-17. The compositions are orally delivered by way of gels, capsules, powders and/or tablets (paragraph 0007). The reference anticipates the instant claims insofar as it discloses a compositions comprising lysine that treats stress-induced diseases such as anxiety disorders.

Claim Rejections - 35 USC § 103 - Obviousness

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schaefer et al. (US 5,505,968).

The reference is discussed above. The reference discloses compositions with a mixture of amino acids but does not provide a composition with a lysine salt combined with additional amino acids such as glutamate or glutamic acid and arginine.

It is *prima facie* obviousness to select a known material based on its suitability for its intended use. See *Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945). Also, established precedent holds that it is generally obvious to add known ingredients to known compositions with the expectation of obtaining their known function. See, e.g., *In re Linder*, 457 F.2d 506, 507 (CCPA 1972); see also *In re Dial*, 326 F.2d 430, 432 (CCPA 1964). It would have been obvious to one of ordinary skill in the art to have combined glutamic acid and arginine to the compositions comprising lysine motivated by the desire to add the ammonia absorbing effect of glutamic acid and arginine for its specific function as supported by cited precedent.

Claims 1-23 are rejected.

Claims 24-26 are withdrawn.

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lezah W. Roberts whose telephone number is 571-272-1071. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Lezah Roberts
Patent Examiner
Art Unit 1614



Frederick Krass
Primary Examiner
Art Unit 1614

